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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/783,092	02/23/2004	Taru Blom	13601-041	3520

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EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
12/03/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/783,092	BLOM ET AL.	
	Examiner	Art Unit	
	SHIRLEY V. GEMBEH	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,7,8 and 14-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-4 and 7-8, 14-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/19/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendments

1. The response filed on **8/27/08** has been entered.

2. Applicant's arguments filed 8/27/08 have been fully considered but they are not deemed to be persuasive.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

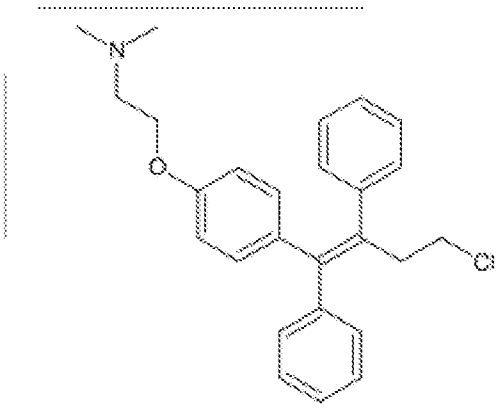
4. Claims 1, 3-4 and 7-8, 14-24 are pending in this office action.
Claim 1 is currently amended and claims 2, 5-6 and 9-13 are cancelled.

5. The information disclosure statement (IDS) submitted on 2/19/08 is acknowledged and has been reviewed.

6. Claims 1, 3-4, 7-8 and 14-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marttunen et al., (1999) and Kangas, (1990) and/or Blom et al., US 6,984665 in view of Fukumitsu et al. (2002) and Crofton et al. (2003) as evidence by Pfeilschifter et al. (2000), for the reasons set forth in the last office action.

Marttunen et al. teach administration of toremifene to patients undergoing cancer treatment with tamoxifene (please note that administration of toremifene metabolizes to

TORE VI, VIII etc as noted by Kangas et al



Toremifene

below). , a compound with the same core structure as compound of formula (1), effects bone in postmenopausal breast cancer patients (wherein bone resorption is a result of drug induced bone turnover) as required by instant claims 1 and 4. See abstract. It is noted that cancer treatment (drug induced) may have a deleterious effect on the acquisition of peak bone mass, which may pose an increased risk of bone fractures as required by instant claims 1 and 22-23. See as evidence by Pfeilschifter et al, (entire ref). Marttunen also teaches the administration of toremifene as 40 mg/day. See abstract as required by instant claims 14-15 and 18-19. However, Marttunen fails to teach the exact claimed compound of instant claim 3, the bone resorption measured as U-NTX as required by instant claim 7-8 or 24, and the specific concentrations of the compound 30, 60 and 90 mg/day as required by instant claims 15-17 and 20-21.

For the above recited deficiency in the teaching of Marttunen, the below references are employed to remedy the deficiency.

Kangas teaches different forms or metabolites of toremefine as TORE, TORE II, V, IV etc for the treatment of breast cancer. See page 9, Fig. I. However, Kangas does not teach the use of these drugs in treating osteoporosis or osteomalacia.

Blom teaches ospemifene for the treatment of osteoporosis (osteomalacia- a bone disease) wherein the ospemifene is administered at a dose of 30-90 mg/day (see col. 7, line 15 and col. 3, lines 40-43). However, Blom does not teach the bone resorption measured as U-NTX, as in instant claims 7-8.

Fukumitsu et al. teach a diagnostic potential of bone resorption marker, type I collagen-cross-linked N telopeptide in urine, wherein the bone resorption is at least 65 nm/mmol creatine (see abstract as required by instant claim 24). The reference also teach one of ordinary skill in the art to use carboxyl terminal propeptide of type I procollagen as an assessment tool in determining bone resorption. See abstract and introduction sec on page, 814. However, Fukumitsu does not teach the compounds, toremifene or ospemifene.

Crofton et al. teach the use of a marker S-PICP measured in both serum of children and post menopausal women, wherein the amount of serum PICP is greater than 180 mg/l. It is therefore assumed that having one of the marker s-PICP greater than 180 mg will therefore have a creatine level of at least 70 as required by instant claims 7-8 and 24. However, Crofton et al. does not teach administering the drugs toremifene or ospemifene.

It would have been obvious to one of ordinary skill in the art at the time of filing Applicants' invention to have administered toremifene for the treatment of osteoporosis

(osteomalcia/ drug induced high bone turnover) because administering toremifene is considered as administering TORE VI, (same as the claimed compound of formula I). Therefore, one of ordinary skill in the art would have been motivated to administer a metabolite of toremifene such as ospemifene (compound of formula I/TORE VI) to patients with increased bone loss because it has been taught by Marttunen because Kangas teaches that metabolites of toremifene are biologically active and resemble toremifene in its hormonal effects.

As to the varying concentration the determination of a dosage having optimum therapeutic index is well within the level of the ordinary skill in the art, and the artisan would be motivated to determine the optimum amounts to get the maximum effect of the drug, hence the reference makes obvious the instant invention.

One of ordinary skill in the art would have been motivated to employ the teachings of Fukumitsu et al. and Crofton for the determination of bone resorption (bone turnover) in a post menopausal patient or osteomalacia at the time of filing the instant application because these techniques are well known in the art for the determination of bone turnover. Thus the combination of both Fukumitsu and Crofton with Marttunen, Blom and Kangas would have been obvious to do. Also, the instant situation is amenable to the type of analysis set forth in In re Kerkhoven, 205 USPQ 1069 (CCPA 1980) wherein the court held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose in order form a third composition that is to be used for the very same purpose since the idea of combining them flows logically from their having been individually taught in the prior art. Applying the same logic

to the instant process claims, given the diagnosing bone resorption, it would have been obvious to use both compounds as a diagnostic tool because the idea of doing so would have logically followed from their having been individually taught in the prior art. Thus, the claimed invention at the time of filing the instant application would have been *prima facie* obvious to make.

7. Claims 1, 3, 7-8 and 14-24 are and is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1- 9 of U.S. Patent Application No. 11/183185. Although the conflicting claims are not identical, they are not patentably distinct from each other. The reasons are as follows:

Both sets of claims refer to treating an individual suffering from increased bone turnover - decrease bone loss in the current application (claim 1) and androgen deficiency (claims 1-9) in the copending application. Thus, the current application's claims anticipate the copending application's claims. As to copending application claims 1-9, these claims refer to treating androgen deficiency in a male with the claimed compound ospemifene with several deficiencies. See copending claim 9 for example where reduced bone density, drug effect are recited.

In view of the foregoing, the copending application claims and the current application claims are obvious variations.

Applicants' amendment to the claim does not overcome the above rejection because, when the specification is used as a dictionary, the compound of formula I is

can also reasonably be used to treat decreased bone density in androgen deficient males.

7. No claim is allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHIRLEY V. GEMBEH whose telephone number is (571)272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, MICHAEL HARTLEY can be reached on 571-272-0616. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. V. G./
Examiner, Art Unit 1618
11/14/08

/Robert C. Hayes/
Primary Examiner, Art Unit 1649